Reduction of Anxiety in Genetically Timid Dogs

Drug-induced Schizokinesis and Autokinesis

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Abstract—In behavior studies of genetically timid and normal dogs it was possible to focus on nervous non-performing animals in a search for agents which might attenuate the overriding anxiety which causes these animals to become rigid, aversive-avoiding or bizarre in the presence of humans. Of the drugs tested, chlordiazepoxide (Librium, Roche), 75 to 200 mg per dog per day, was most effective in alleviating the anxious condition. Sometimes the drug had the effect of getting the animal over a "threshold" so that he continued to perform (bar-pressing) indefinitely after once started through the aid of chlordiazepoxide. This is considered an example of both schizokinesis and autokinesis which Gantt first described and associated with drug action utilizing conditional response techniques.

IN BEHAVIOR STUDIES of genetically timid and normal dogs it has been possible to utilize the most nervous animals as a model for screening agents which might attenuate severe anxiety. The animals display their timidity in rather obvious ways some of which can be measured—they may become rigid in the skeletal muscle system, often show spasmodic jerking, and try to hide, etc. Most of these symptoms are displayed at the approach of a human, though a novel stimulus such a fire extinguisher, broom or an umbrella may induce these responses. While most breeders actively discard these animals, our laboratory has selectively bred these abnormal extremes for study. Many investigators have shown heredity to be important in normal and abnormal behavior (Scott and Fuller, 1965; Hirsch, 1963; Broadhurst, 1960). We chose a single breed, the short-haired pointer, and began our studies two months after the birth of the dogs in our laboratory.

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While we have been successful in producing nervous animals, we have begun only recently to seriously try and attenuate the condition with behavioral and/or pharmacologic means. The study reported here involves three attempts to test the effectiveness of some widely used psychoactive drugs as well as some compounds under development in attenuating the condition of these animals. The results support Gantt's concepts of schizokinesis and autokinesis (1953). These concepts are now well known as a basic splitting or lack of integrative harmony of subsystems within a whole (schizokinesis), and the self-determined autonomous development which such subprocesses or subsystems sometimes display (autokinesis). These subsystems which Gantt considered as neurological have forcelike attributes (kinesis). That a psychoactive drug may impose a schizokinesis or even a condition of autokinesis was also first expounded by Gantt (1968, 1970).

Method

Experiment I: (double blind)

Twenty dogs with varying degrees of timidity were randomly divided into four groups yet equated in nervousness by utilizing a table of random numbers. Baselines were obtained and daily medications were begun each morning, five days per week as follows:

100 mg chlorpromazine (neuroleptic—a major phenothiazine tranquilizer)
400 mg imipramine (tricyclic antidepressant)
200 mg chlordiazepoxide (angiolytic bendiazepine—minor tranquilizer)
Placebo pills similarly administered to controls

Animals were behaviorally tested weekly before, during, and after the two week treatment period. The tests included reaction to a loud sound (122 decibels), reaction to humans and brief exploratory activity in an empty room. In addition a rating scale yielding a nervous score was completed on each animal. The actual score being the sum of the number of nervous behavioral aspects checked as present. Factors contributing to the nervous score included avoidance of humans, freezing, urinating, etc.

Experiment II:

Twenty animals were randomly divided into two groups one of which was medicated daily for one week for each compound studied. Medications, which were orally administered daily at 9 AM,

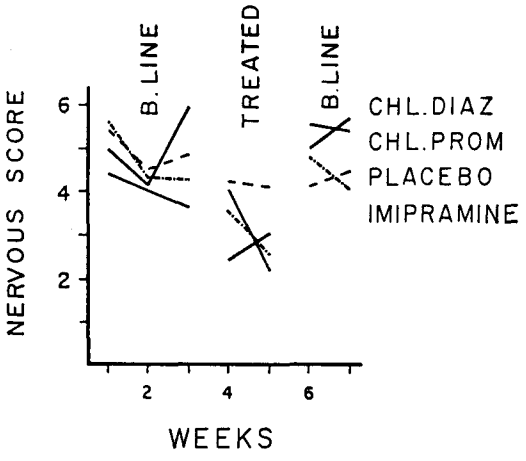

FIG. 1. Nervous score as measured each week for four groups of nervous dogs: 3 medicated groups and 1 placebo group. Chlordiazepoxide, chlorpromazine, placebo and imipramine labels appear in the chart opposite their final data plot (seventh week).

were as follows: experimental compound (Wallace Laboratories), 1200 mg; meprobamate, 1200 mg; chlordiazepoxide, 75–100 mg. Behavior tests were done each Friday for the next eight weeks while the compounds and placebo were administered (Figs. 4, 5 and 6).

Experiment III:

Fifteen dogs too nervous to perform simple bar-pressing were faced with the task again with seven receiving chlordiazepoxide (75 mg/dog) and the remaining eight serving as non-medicated controls. Each pressing of the bar automatically yielded food. If they still failed to perform, the animals were placed back in an outside bin similar to their living quarters, alleviating the stress of unfamiliarity, and the bar-pressing equipment was brought to them. It is well known that removing our timid animals from their home bins to our experimental laboratory room can be very upsetting. Chlordiazepoxide was continued in the treated group throughout the bar-pressing attempts. In addition, nonperforming animals were given an isolated oral dose to determine if this one drug treatment would induce the adaptive bar-pressing—in retrospect an opportunity for autokinesis.

Results

The psychoactive compounds of chlorpromazine, chlordiazepoxide and imipramine reduced the nervous score more than placebo during the treatment period (Fig. 1). The nervous score decreases rather obviously for the treated groups.

In brief exploratory activity (Fig. 2) which is normally depressed in nervous animals, chlordiazepoxide reduces the sound-

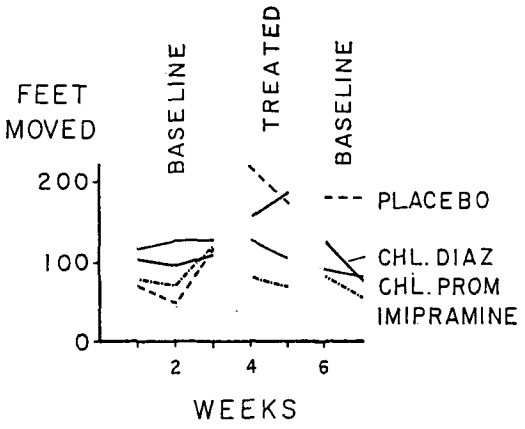

FIG. 2. Mean distance traversed during 2-minute activity test in empty room for 4 groups of dogs. Drug labels are opposite the data plot for the final (seventh) week.

induced "freeze" or time of immobility to less than half the untreated level and does so better than the other medications. Figure 4 shows a "release to explore" for the medicated animals receiving the experimental compounds, particularly chlordiazepoxide but not meprobamate. Figure 5 shows the increase in number of dogs approaching the human for the medicated group when they receive chlordiazepoxide. Note that neither the control group nor the medicated group when receiving other medications were improved in this regard. The numbers of dogs in Experiment II "freezing" to to the loud horn reaches the lowest point for the animals receiving chlordiazepoxide (Fig. 6).

Animals which were faced again with bar-pressing procedures in a typical operant conditioning task failed again in the isolation chamber unless medicated. However, when asked to do the bar-pressing in the outside bin, most animals finally performed as shown in Figure 7. Note though that drugged animals do better (dotted lines) and that if an animal has not been performing for a considerable number of days—apparently due to anxiety concerning the ap-

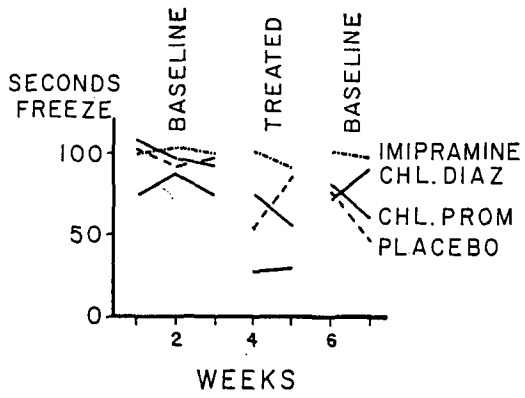

FIG. 3. Mean freezing time (time of immobility) as measured each week for 3 treated and 1 placebo group of dogs. Note superiority of chlordiazepoxide during treatment period.

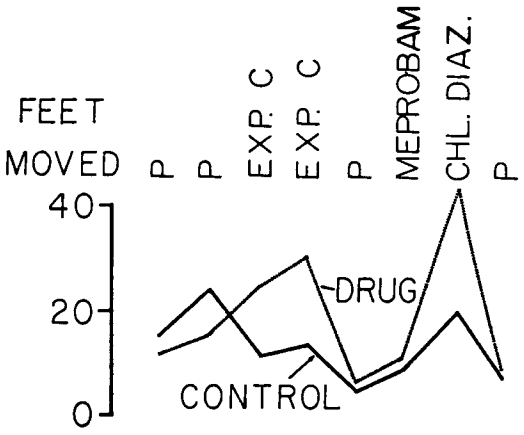

FIG. 4. Mean distance traversed during 2-minute exploratory activity each week in empty room for 2 groups of 10 dogs each. Treatment (dotted line) for the drug group included: P = placebo; Exp. C. = experimental compound; meprobamate, 1200 mg/day; chlordiazepoxide, 75–100 mg/day.

paratus and situation—he often can be made to perform with a single dose of chlordiazepoxide. This is indicated by the short segments of dotted lines showing where medication was administered to the dog in the heretofore non-medicated group. Thereafter many animals continued to perform.

Discussion

Drug Effects as Schizokinesis and Autokinesis

Gantt (1968, 1970) pointed out the innate schizokinetic action of a large number of psychoactive drugs using the more objective method of conditioned response. The data reported here are gross behavioral measures or operant conditional responses, but they are completely consistent with his more physiological experiments.

Psychoactive drugs and those affecting more peripheral regions

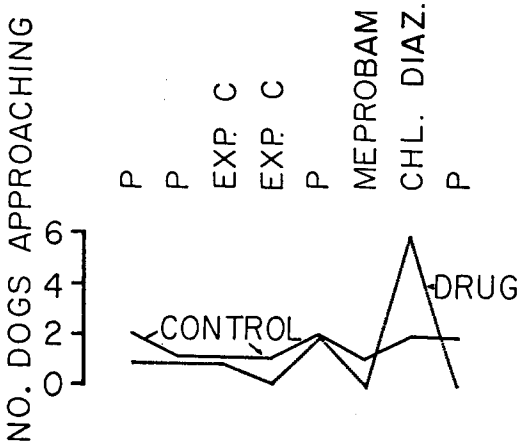

FIG. 5. Week-by-week determination of number of dogs approaching human during 30 seconds time limit. (two groups of 10 dogs each. P = placebo).

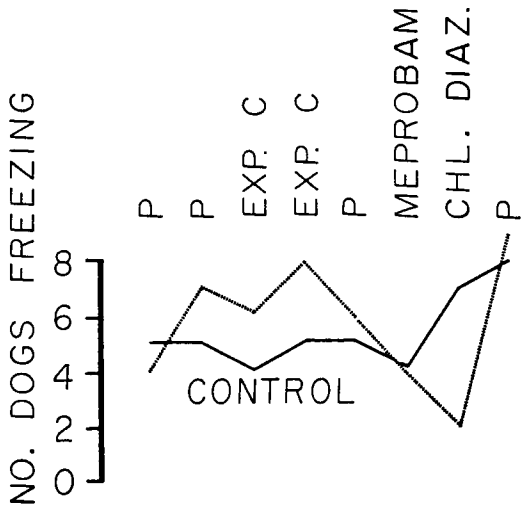

FIG. 6. Number of dogs "freezing" (remaining immobile) for 2 minutes after 1-second blast of 122 decibel Klaxon.

of the CNS are neurologically biased in their action, *i.e.*, induce schizokinesis. Many of these drugs have been noted as "specific" in their action: as sympthomimetic, para-sympathomimetic, etc. The terms tend not to convey the force-like vector as the term "kinesis" does. Neurotic dogs are schizokinetically unbalanced already—thus an oppositely biased or counter-schizokinesis—inducing drug could, if appropriate, stabilize such a system.

If a drug starts processes which improve the balance and integrative functioning of the organism, we have what Gantt called autokinesis. It is positive in nature provided these processes grow and continue without further environmental input (Gantt, 1953). If the processes initiated go in a deteriorating direction, then the

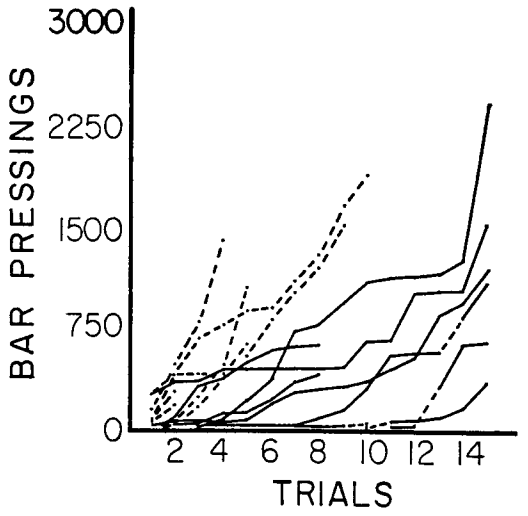

FIG. 7. Individual cumulative bar-pressing record for dogs receiving chlordiazepoxide, 75–100 mg/day (broken lines) and for non-medicated animals. Single medication of non-drugged group is shown by broken line segments.

autokinesis is negative. It is interesting that the essential nature of both positive and negative autokinetic processes is characterized by the cybernetic attribute of positive feedback. Positive feedback, however, if continued leads to breakdown and therefore may be true only for the early history of the changing system displaying positive autokinesis. A cybernetic or systems theory analysis of schizokinesis and autokinesis would be enlightening and probably provoke intriguing hypotheses for reasearch.

Conclusions

Chlordiazepoxide has consistently been effective in attenuating anxiety in genetically timid dogs. A "threshold" effect has sometimes been obtained wherein previously nervous non-performing animals could be made to start performance which continued even though the drug is withdrawn. Gantt's concepts of schizokinesis and autokinesis focusing as they do on the disharmony and autonomous changes which can characterize subsystems within the whole seem the most appropriate for understanding man aspects of CNS-acting drugs. Further, the animals' hyper-responsiveness to the environment and their maximum improvement with chlordiazepoxide confirms our impression that fear or anxiety is their main handicap.

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